Annals of Clinical and Analytical Medicine
Original Research

Pre-Endoscopic viral screening of children during the Covid-19 pandemic

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Abstract
Aim: Transmission of SARS-CoV-2 infection can easily occur through direct or close contact with infected people, just as with other infectious diseases. Therefore, it is important to detect it prior to the intervention for protecting the health of both the healthcare worker and the patient. In the study, it was aimed to determine the seropositivity rates of acute respiratory syndrome coronavirus 2, hepatitis A, hepatitis B, hepatitis C virus and human immune deficiency virus infections among children who underwent gastrointestinal endoscopy.
Material and Methods: The study was conducted at the Department of Pediatric Gastroenterology of the Karabuk University in Turkey from December 2020 to December of 2021. A total of 175 children were included in the study. The study was divided into three age groups as follows: 1-6 years old, 7-12 years old and 13-18 years old. All children were screened for acute respiratory syndrome coronavirus 2, hepatitis A, hepatitis B, hepatitis C virus and human immune deficiency virus infections.
Results: The median age was 12.5 years (1-18). The seroprevalence of acute respiratory syndrome coronavirus 2, Anti-HAV IgM, Anti-HAV IgG, HBsAg, Anti-HBs, Anti-HCV, Anti-HIV and were detected 0.57%, 0.57%, 42.8%, 0%, 58.8%, 1.1% and 0 % respectively. The seroprevalence of Anti-HAV IgG was significantly higher in children aged 1-6 years than in the group aged 13-18 years (95.7 vs 25.2: $x2=48.1$, $p=0.001$).
Discussion: Although seroprevalence rates prior to endoscopy were low in this study, viral screening, except for hepatitis A infection, is essential for the safety of both patients and healthcare.

Keywords
Endoscopy, Hepatitis, HIV; SARS-CoV-2, Screening

DOI: 10.4328/ACAM.21037 Received: 2021-12-31 Accepted: 2022-02-08 Published Online: 2022-02-09 Printed: 2022-03-01 Ann Clin Anal Med 2022;13(3):325-329
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Introduction

Viral hepatitis poses a significant burden for both children and adults worldwide. Although hepatitis B (HBV) and hepatitis C (HCV) infections in adults are among the most common chronic viral infections worldwide, they are rare in childhood [1]. In contrast to HBV and HCV, hepatitis A (HAV) infection, which is generally asymptomatic is the most common cause of childhood hepatitis, especially in underdeveloped and developing countries [2]. Just like viral hepatitis, the human immunodeficiency virus (HIV) infections are a global public problem around the World [3].

It has been known for a long time that infections and diseases can easily spread through the blood and some body fluids and are important risk factors for healthcare workers. Considering the direct transmission of microorganisms such as HBV, HCV, HIV, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) /COVID 19 and some bacterial agents from the patient to healthcare workers [4-6], routine serological tests for the presence of infective pathogens before endoscopy and surgical procedures play an important role in the protection of healthcare workers [6].

Although pre-endoscopic screening for HBV, HCV and HIV is routinely performed in almost all endoscopy centers in the world, very few studies have been reported on SARS-CoV-2 screening and these studies were done in adults [7,8].

Therefore, the purpose of the present study was twofold: (1) to determine the seroprevalence of HAV, HBV, HCV, HIV and SARS-CoV-2 in children who underwent endoscopy; (2) to investigate whether SARS-CoV-2 infection and Hepatitis A tests have a routine place as a screening test in children prior to endoscopy. To our knowledge, this is the first study to investigate the seroprevalence of HAV, HBV, HCV, HIV and SARS-CoV-2 in children undergoing endoscopy.

Material and Methods

The cross-sectional study was conducted at the Department of Pediatric Gastroenterology of the Karabuk University Hospital in Turkey from December 2020 to December 2021. The study population consisted of 175 children who underwent upper and lower gastrointestinal (GI) endoscopy. The participants were divided into three age groups as follows: 1-6, 7-12 and 13-18 years old.

The children undergoing GI endoscopy were screened for HAV, HBV, HCV, HIV and SARS-CoV-2 infections. The screening for Anti-HAV IgM, Anti-HAV IgG, HBsAg, Anti-HBs, Anti-HCV and Anti-HIV was carried out using enzyme-linked immunosorbent assay (ELISA) Architect I2000SR (Abbott Diagnostic, USA). Nasal swabs for SARS-CoV-2 test from children were taken by an experienced nurse 24 hours prior to endoscopy. Nasopharyngeal samples were tested by CFX96 Touch Real-Time PCR Detection System-Bio-Rad, Turkey. If any of the serological indicators was positive, the result was accepted as "seropositivity", if all serological indicators were negative, the result was accepted as "seronegativity".

Statistical Analysis

The data were analyzed with SPSS version 21.0 software for Windows. Numerical variables were expressed as median (min-max), and categorical variables were expressed as percentages. The Kolmogorov-Smirnov test was carried out to determine the normality of data distribution. Age, Anti-HAV IgM, Anti-HAV IgG, HBsAg, Anti-HBs, Anti-HCV, Anti-HIV and SARS-CoV-2 had abnormal data distribution. Comparison of categorical data was carried out with the chi-square test. A p- value of less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the Turkish Health Ministry Ethical Review Committee (No. 2021/770). All participants' parents provided written informed consent.

Results

The median age of 175 children was 12.5 years (1-18). Of the 175 children, 118 (66.7%) were female and 57 (33.3%) were male. All children were vaccinated against hepatitis B, 122 of them (69%) were vaccinated against hepatitis A. The study was divided into three age groups as follows: 1-6 years old (13.1%), 7-12 years old (21.1%) and 13-18 (65.8%) years old. The Anti-HAV IgM, Anti-HAV IgG, HBsAg, Anti-HBs, Anti-HCV, Anti-HIV and SARS-CoV-2 seropositivity were detected 1 (0.57%), 75 (42.8%), 0 (%0), 103 (58.8%), 2 (1.1%), 0 (0 %) and 1 (0.57%), respectively (Table 1).

Of the 175 children, 1 (0.57%) was positive for SARS-CoV-2. Anti-HAV IgG seroprevalence according to the age groups 1-6, 7-12 and 13-18 years old were 95.7%, 64.9% and 25.2%, respectively. Anti-HAV IgG seropositivity was significantly higher in children aged 1-6 years than in the group aged 13-18 years (95.7 vs 25.2: $x2=48.1$, $p=0.001$). A decrement in Anti-HAV IgG seropositivity with age was found in older age groups. Seropositivity rates by age group are presented in Table 2. No significant differences in overall Anti-HAV IgM, Anti-HAV IgG, HBsAg, Anti-HBs, Anti-HCV, Anti-HIV and SARS-CoV-2 seropositivity rates were observed between females and males (Table 3).

Discussion

Screening for HAV, HBV, HCV, HIV, in addition to the SARS-CoV-2 virus, which causes pandemic all around the world, before interventional procedures such as endoscopy is particularly important for preventing infectivity and transmission [5,9]. In this study, HBsAg and anti-HIV seropositivity were not detected in any of the patients aged between 1-18 years. Besides the seropositivity rates for Anti-HAV IgM, Anti-HAV IgG, Anti-HBs, Anti-HCV and test positivity rate of SARS-CoV-2 were detected as 0.57%, 42.8%, 58.8%, 1.1% and 0.57%, respectively.

According to the World Health Organization (WHO) data, HAV, which can be sporadic or epidemic, affects 1.4 million people annually [2,10]. According to WHO data, Turkey is among the middle-level endemic countries with a seropositivity rate of 70% of the population under 30 years old. However, HAV seropositivity rates vary between regions in our country [10]. In a study byAriyarathna et al., in Sri Lanka with 1403 children, the rate of anti-HAV IgG seropositivity between the ages of 1-10 and 11-20 were reported as 70.4% and 66.8%, respectively [11]. In a study by Hayajneh et al. (2015) in Jordan, HAV seroprevalence rates among the age categories of 2-4 years, 5-9 years, 10-14 years and 15-19 years were reported as 32%, 44%, 63% and 78%, respectively, and reported the need for a more comprehensive and effective vaccination [12]. On the

Table 1. Seroprevalence of SARS-CoV-2, HAV, HBV, HCV and HIV prior to endoscopic procedures.

	SARS-CoV-2	Anti-HAV IgM	Anti-HAV IgG	HBsAg	Anti-HBs	Anti-HCV	Anti-HIV
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Positive	1	1	75	0	103	2	0
Negative	174	174	100	175	72	173	175

SARS-CoV-2: Severe Acute Respiratory Syndrome CoronaVirus 2, HAV:Hepatitis A virus, HBV:Hepatitis B virus, HCV:Hepatitis C virus, HIV: Human immunodeficiency virus

Table 2. Seropositivity rates of SARS-CoV-2, HAV, HBV, HCV and HIV according to age groups.

Age	SARS-CoV-2	Anti-HAV IgM	Anti-HAV IgG	HBsAg	Anti-HBs	Anti-HCV	Anti-HIV
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1-6 years	0	0	22*	0	19	0	0
7-12 years	1	0	24	0	18	0	0
13-18 years	0	1	29*	0	66	2	0

* Anti-HAV IgG seropositivity x2 (overall) = 48.1, p = 0.001 in children aged 1-6 years than in 13-18 years age group, SARS-CoV-2:Severe Acute Respiratory Syndrome Corona Virus 2, HAV:Hepatitis A virus, HBV:Hepatitis B virus, HCV:Hepatitis C virus, HIV: Human immunodeficiency virus. Severe Acute Respiratory Syndrome Corona Virus 2

Table 3. Comparison of seropositivity rates of SARS-CoV-2, HAV, HBV, HCV and HIV by gender.

Gender	SARS-CoV-2	Anti-HAV IgM	Anti-HAV IgG	HBsAg	Anti-HBs	Anti-HCV	Anti-HIV
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Male	1	0	29	0	31	0	0
Female	0	1	46	0	72	2	0

SARS-CoV-2: Severe Acute Respiratory Syndrome CoronaVirus 2, HAV:Hepatitis A virus, HBV:Hepatitis B virus, HCV:Hepatitis C virus, HIV: Human immunodeficiency virus

other hand, in the study by Atik et al. in 2021, the rate of anti-HAV IgG seropositivity between the ages of 0-10 and 11-17 were reported as 63.1% and 38.8%, respectively [13]. Although studies from both Turkey and the world have not evaluated children before endoscopy, our study found a statistically significant increase for the anti-HAV IgG seropositivity rate in children between the ages of 1-6 when compared with children aged between 13-18, and we also determined that the seroprevalence decreases with increasing age (95.7% between the ages of 1-6, 64.9% between the ages of 7-12, 25.2% between the ages of 13-18) (p=0.001). Both the results of this study and the results reported by both Ariyarathna and Atik, support the point of view that "Anti-HAV IgG seroprevalence decreases with increasing age".

Screening of cases for HBV and HCV infections before invasive procedures such as endoscopy and surgical procedures, early diagnosis and preventing transmission by horizontal route are important both for health service providers and for public health [1,2,5].

In the study by Jemilohun et al., which included 432 patients who underwent endoscopy in Nigeria in 2019, the prevalence of HBV, HCV and HIV were reported as 4.3%, 2.1% and 1%, respectively [5]. In the study by Gańczak et al., which included 1652 patients in Poland, it was reported that anti-HIV positivity was not detected in any of the patients, and the prevalence of HBsAg and anti-HAV were 0.6% and 0.9%, respectively [14]. In the study by Deveci et al., HBsAg seropositivity was reported as 0.3% before the endoscopy procedure in Elazig, and the seropositivity rates according to the age groups were reported as 15.9% for 1-4 years old, 27.6% for 5-9 years old, 31.7% for 10-14 years old and 19.4% for 15-18 years old. In the same study, the seropositivity rate of anti-HCV was reported as 0.3% [15]. In the seroprevalence study by Cifci et al., with patients who underwent upper GI endoscopy in Konya, the seropositivity rates of HBsAg and anti-HCV were reported as 2.9% and 0.5%, respectively [16]. While we did not detect any HBsAg seropositivity in our study, Jemilohun et al. (4.3%), Gańczak et al. (0.6%), and Ciftci et al. (2.9%) reported higher rates in their studies that were conducted with adults different from our study. It was thought that this difference was due to the difference in distribution between the age groups of patients included in the study, as well as the role of vaccination of the patients included in the study.

The mean value of anti-HBs seropositivity was determined as 58.8% in our study. On the other hand, seropositivity rates among the age groups were determined as 82.6% for the 1-6 age group, 48.6% for the 7-12 age group, 57.4% for the 13-18 age group. We found that the highest rate of anti-HBs seropositivity was in the 1-6 age group. In the same center, between January 2015 and December 2016, we found the seropositivity rates of 0.2% for HBsAg, 61.1% for anti-HBs and 0.1% for anti-HCV in children aged between 0-18 years. According to age subgroups, we reported the seroprevalence rates for anti-HBs as 77.8% between 0-1 years, 71.3% between 2-6 years and 57.9% between 7-18 years of age [17].

In our seroprevalence study, we found that the rate of seropositivity for anti-HBs increased over the years. We found that the seroprevalence positivity rates in our study were higher than the rates reported by Deveci et al. It was thought that the difference in anti-HBs positivity rates might be due to differences in the regions where the studies were carried out, distribution of cases according to age groups and differences in the socio-economic levels of the groups. These results show that routine hepatitis B vaccination is applied effectively.

We found in our study that the seropositivity of anti-HCV was 1.1% in the tests performed before endoscopy in children aged

between 1-18 years. While the rate in the study by Jemilohun et al. (2.1%) with adult patients was higher than in our study, Gańczak et al. (0.9%) and Cifci et al. (0.5%) reported similar rates with our study. Besides, Deveci et al., reported a lower rate of anti-HCV in their study with the childhood age group (0.3%) when compared with the results of our study. The difference in rates was thought to be due to differences between age groups in addition to regional differences.

Tests before interventional procedures (endoscopy, surgery, etc.) help in the early diagnosis of undiagnosed HIV infected patients, and are important for preventing infectivity and transmission [3,6]. In a study by Saltzman et al., in the USA, the rate of transmission by mucocutaneous spread for HIV infection was reported as 0.1% [18]. In another study by Caillot et al., in France, it was reported that the lifetime risk of HIV infection of the person performing the interventional procedure was 0.15% [19]. Kırgezen et al. reported that 0.2% of the patients who underwent tonsillectomy included in the study had anti-HIV seropositivity [20]. In studies of Tekin et al., [21] and Deveci et al. [15], anti-HIV seropositivity was not reported in any of the children. In our study, similar to the result of Tekin et al., and Deveci et al., HIV positive case was not detected. Besides, these rates were also lower than the results of studies conducted in high-risk countries for HIV.

SARS-CoV-2 is transmitted by droplet route and by contact with virus-contaminated surfaces. Transmission has also been demonstrated during the incubation period in individuals who are asymptomatic or have symptoms of the disease [6,9]. The identification of asymptomatic cases with a positive SARS-CoV-2 PCR test will provide significant benefits in protecting the health of both the patient and healthcare professionals. In addition, pre-endoscopic SARS-CoV-2 screening is important for the prevention of contagiousness.

In a multi-center study in Spain by Hernández et al., the rate of antibody positivity in tests that were performed before the endoscopic procedure was 1.9% in 211 patients who underwent endoscopy. In addition to that, they reported that SARS-CoV-2 PCR positivity was not detected in any of these patients [22]. In the study by Lin et al., a total of 1295 pediatric patients in 3 different hospitals in the USA were included and the rate of SARS-CoV-2 PCR test positivity was reported as 0.93% [9]. In another study by Bloom et al., in the USA, it was reported that the SARS-CoV-2 test was positive in 3.6% of the adult patients without any symptoms in pre-operative screening tests [23]. In the study by Singer et al. in the USA, which included 4739 patients of all age groups without preoperative symptoms, it was reported that the SARS-CoV-2 PCR test result was positive in 0.13% of the cases [24]. In another study by Azılı et al., in which cases under the age of 18 who had no preoperative history, symptoms or signs for COVID-19 were included, it was reported that 0.9% of the cases had positive SARS-CoV-2 PCR test results [25].

In our study, we found a positive SARS-CoV-2 PCR test result in 0.57% of children aged between 1-18 years who had no symptoms before the endoscopy procedure. In studies conducted by Hernández et al. (1.9%), Lin et al. (0.93%) and Azılı et al. (0.90%), when vaccination programs were not implemented at the beginning of the pandemic, SARS-CoV-2 PCR test results were found to be relatively higher than the rate we found in our study conducted in the 2nd year of the pandemic. On the other hand, the result (0.13%) was relatively low in the study of Singer et al., which covered all age groups compared to the result of our study, and we thought that this difference might be due to the difference in age distribution between these studies.

The most important limitation of this study is the presence of the limited number of studies about COVID-19 in children. Therefore, we compared our results with a limited number of studies. The second limitation is that we could not measure neutralizing antibody level against SARS-CoV-2 infection due to funding problems. Another limitation is that the results of this study cannot be generalized since it is a single-center study.

Conclusion

Despite limitations, the present study revealed that the seropositivity rates of SARS-CoV-2 and Anti-HAV IgM were extremely low in children who underwent endoscopy. Even though the seroprevalence rate of SARS-CoV-2 was low in the study, just as other viral hepatitis and HIV, routine screening of the SARS-CoV-2 prior to the endoscopic procedure can help prevent transmission of the virus between patients and healthcare workers in healthcare facilities. Moreover, the study demonstrated that there is no need for routine Anti-HAV screening prior to endoscopy procedure as the children have a high anti-HAV seroprevalence rate.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None*

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:
Erkan Dogan, Eylem Sevinc, Nergiz Sevinc, Erhan Basar. *Pre-Endoscopic viral screening of children during the Covid-19 pandemic. Ann Clin Anal Med 2022;13(3):325-329*